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## **Optimising peri-operative care to prevent Acute Kidney Injury**

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Post-operative acute kidney injury (AKI) is a common complication of surgery. Rates vary according to type of surgery ranging from 13% following GI surgery and 10% after orthopaedic surgery to 26% following cardiac surgery to [1-3].

Understanding the aetiology of post-operative AKI is vital to peri-operative optimisation. However, the pathogenesis is complex and usually multifactorial (Figure 1). Renal hypoperfusion plays an important role in post-operative AKI. This can occur as a result of a number of different factors including hypovolaemia, loss of autoregulation during anaesthesia, cardiogenic shock, sepsis and high risk medicines such as non-steroid anti-inflammatory drugs (NSAIDs) and inhibitors of the renin-angiotensin system.

Cardiac surgery is associated with particularly high rates of AKI. Contributing factors unique to cardiac surgery include the use of intra-aortic balloon pumps and cardiopulmonary bypass (CPB). CPB can lead to AKI through a number of mechanisms. These include inflammation, ischemia reperfusion injury and haemodilution. Contact of blood products with the CPB circuit leads to a systemic inflammatory response and ischaemia reperfusion injury. The shear stress also incites red cell lysis and release of free haemoglobin which subsequently releases iron in the presence of oxidants causing tissue damage. Haemodilution from priming of the CPB circuit is also associated with AKI. This is thought to be due to reduced oxygen delivery. Finally, cholesterol emboli can occur from aortic manipulation and clamping during CBP.

The importance of preventing post-operative AKI has been highlighted by the increasing observational data demonstrating adverse outcomes in patients with even mild, transient episodes of AKI. These include increased mortality, increased risk of

developing chronic kidney disease and longer hospital in-patient stays with resulting economic implications [1, 2].

Identifying patients at high risk of AKI facilitates closer monitoring allowing for peri-operative optimisation. Several validated risk scores have been developed for use in patients undergoing cardiac surgery. Fewer risk scores have been developed for patients undergoing non-cardiac surgery. Most of these risk scores include both patient and operation related risk factors with the most common risk factors shown in Figure 1. There is, however, a lack of defined interventions once these patients have been identified.

Multiple pharmacological agents have been studied in the peri-operative period. Loop diuretics have consistently been shown to offer no benefit and possibly harm and so are not recommended unless in the context of fluid overload. Vasodilator therapy such as dopamine, fenoldopam and atrial natriuretic peptide (ANP) were thought to be beneficial as they increase glomerular filtration rate through renal vasodilation and natriuresis. Once again this benefit has not been shown in clinical studies with the possibility that these agents may even lead to harm[4]. Similarly, N-acetylcysteine, 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase inhibitors (statins), aspirin and clonidine have been shown to be ineffective.

Whilst there are a lack of interventions that reduce the risk of AKI, there is evidence to suggest that avoidance of certain medications in the peri-operative period may reduce the risk of post-operative AKI. NSAIDs are effective analgesics commonly used to treat post-operative pain but can lead to AKI through inhibition of prostaglandins leading to loss of afferent arteriolar vasodilation. Similarly, aminoglycosides use in the peri-operative period has been associated with increased

rates of AKI even at low doses used as surgical prophylaxis [5]. There is conflicting evidence with regards to the avoidance of inhibitors of the renin–angiotensin system in the peri-operative period with studies showing that continuation may in fact lower rates of AKI[6]. These data are largely observational thereby subject to confounding. In the absence randomized control trial evidence and their well described effects on glomerular filtration rate, it would seem logical to withhold these agents in the peri-operative period. The use of contrast media in the peri-operative period is more controversial with increasing evidence suggesting that the risks of intravenous contrast are overstated[7]. Therefore, there appears to be no need to limit CT scan quality by avoiding the administration of contrast media in the peri-operative period.

Peri-operative haemodynamic optimization to maintain renal perfusion is an important means of preventing post-operative AKI. Periods of intra-operative hypotension with a mean arterial pressure (MAP) of less than 60mm Hg are associated with increased rates of AKI. However, it is important to note that fluid overload is associated with increased mortality and aggravate AKI by causing a reduction in GFR through increased subcapsular pressure and abdominal compartment syndrome[8]. Striking the balance between adequate fluid resuscitation whilst avoiding fluid overload is important in the peri-operative period but often difficult to achieve in practice.

Choice of intravenous fluid therapy is emerging as an important factor in the development of post-operative AKI. Hydroxyethyl starches have been associated with AKI in several studies and so their use is no longer recommended in any context [9]. There is also concern regarding the high chloride content of 0.9% saline which has been associated with hyperchloremic acidosis, renal vasoconstriction

and AKI [10]. These concerns have led to the increasing use of balanced crystalloid solutions.

Two recent studies have evaluated the effect of a “KDIGO bundle” in patients defined as high risk using the urinary biomarker (inhibitor of metalloproteinase-2 x insulin-like growth factor-binding protein 7) [TIMP-2]·[IGFBP7] >0.3. This bundle comprises of optimization of volume status and haemodynamics and avoidance of nephrotoxic drugs. Meersch et al found reduced rates and severity of AKI in patients undergoing cardiac surgery compared to standard care[11]. Similarly, a study of patients undergoing major abdominal surgery showed reduced rates, severity of AKI, and length of hospital stay following implementation of this care bundle[12]. However, this biomarker is not currently in routine use but may provide a future means of risk stratification coupled with an effective intervention. Further studies are required to confirm these findings.

## **Conclusion**

Surgery is an important cause of AKI and is associated with adverse outcomes. Identifying patients at high risk of AKI may allow for peri-operative optimisation and closer monitoring. Biomarkers are emerging as a potentially important tool in early risk stratification. There are no pharmacological agents that reduce or prevent post-operative AKI. Identification of high risk individuals, haemodynamic optimization and careful fluid balance management, avoidance of high risk medicines in the peri-operative period and monitoring of renal function are likely to be beneficial.

## **Conflict of Interest Statement**

The authors declare no conflict of interest.

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